Serial No.: 08/479,995

Filed: June 7, 1995

Page 2 [(Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

PLEASE AMEND THIS APPLICATION AS FOLLOWS:

In the Claims:

Amend claims 283-294, 360-361, 411-417, 464-475 and 479-485 as follows:

283. (Twice Amended) A composition of matter comprising:

a first part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and



a second part which comprises one or more <u>non-radioactive</u> signalling entites substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

284. (Twice Amended) A composition of matter comprising:
a first part which comprises an analyte having one or more molecularly recognizable portions thereon;

a second part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, and a second portion comprising one or more nucleic acid sequences or segments; and

a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion or portions on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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285. (Twice Amended) A composition of matter comprising: a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

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one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

286. (Twice Amended) A composition of matter comprising: a complex which comprises:

an analyte having one or more molecularly recognizable portions thereon;

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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287. (Twice Amended) A composition of matter comprising:

a first part which comprises more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

a second part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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288. (Twice Amended) A composition of matter comprising: a first part which comprises an analyte having one or more molecularly

recognizable portions thereon;

a second part which comprises more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion and a second portion comprising one or more nucleic acid sequences or segments; and

a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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289. (Twice Amended) A composition of matter comprising: a complex which comprises:

> more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more non-radioactive signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

290. (Twice Amended) A composition of matter comprising: a complex which comprises:

an analyte having one or more molecularly recognizable portions thereon;

more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more non-radioactive signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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291. (Amended) A composition of matter comprising:

a first part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

a second part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of providing a detectable signal.

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292. (Amended) A composition of matter comprising:

a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of providing a detectable signal.

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293. (Amended) A composition of matter comprising:

a first part which comprises an analyte having one or more molecularly recognizable portions thereon;

a second part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

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a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of providing a detectable signal.

294. (Amended) A composition of matter comprising:

a complex which comprises:

an analyte having one or more molecularly recognizable portions thereon;

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of providing a detectable signal.

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360. (Twice Amended) An article of manufacture comprising:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

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more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequences or segments, and one or more [non-radioactive] signal generating portions, each capable of providing a detectable signal.

361. (Twice Amended) An article of manufacture comprising:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequences or segments, and [non-radioactive] one or more polynucleotides which have been chemically modified or artificially altered.

411. (Twice Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:



- (i) a container carrying a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable portion on said analyte, and a second portion comprising one or more nucleic acid sequences or segments; and
- (ii) a container carrying more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequence or segment, and one or more [non-radioactive] signal generating portions, each such portion being capable of providing a detectable signal.

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412. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a container carrying a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable portion, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion, and one or more signal generating portions, each such portion being capable of providing a detectable signal.

413. (Twice Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a container carrying more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

a container carrying more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion to form a polynucleotide hybrid, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

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414. (Twice Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

sequences or segments, and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more [non-radioactive] signal generating portions capable of providing a detectable signal.

415. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a complex which comprises:

- (i) more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and
- (ii) more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of providing a detectable signal.

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416. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more polynucleotides which have been chemically modified or artificially altered.

417. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion to form a polynucleotide hybrid, and one or more polynucleotides which have been chemically modified or artificially altered.

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464. (Amended) A composition of matter comprising:

a first part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a second part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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Page 13 [(Amendment Under 37 C.F.R. §1.115

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465. (Amended) A composition of matter comprising:

a first part which comprises an analyte having one or more molecularly recognizable portions thereon, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof:

a second part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognzable portion or portions on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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Page 14 [(Amendment Under 37 C.F.R. §1.115

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466. (Amended) A composition of matter comprising: a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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467. (Amended) A composition of matter comprising:

a complex which comprises:

an analyte having one or more molecularly recognizable portions

thereon;

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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(In Response To The October 27, 1999 Office Action) - August 25, 1999]

468. (Amended) A composition of matter comprising:

a first part which comprises more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a second part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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469. (Amended) A composition of matter comprising:

a first part which comprises an analyte having one or more molecularly recognizable portions thereon;

a second part which comprises more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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470. (Amended) A composition of matter comprising: a complex which comprises:

more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more non-radioactive signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble

phase.

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471. (Amended) A composition of matter comprising:

a complex which comprises:

an analyte having one or more molecularly recognizable portions thereon;

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more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable analyte portion, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said more than one bridging entity nucleic acid second portion, and one or more signal generating portions capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble

phase.

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472. (Amended) A composition of matter comprising:

a first part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a second part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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473. (Amended) A composition of matter comprising:

a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more non-radioactive signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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474. (Amended) A composition of matter comprising:

a first part which comprises an analyte having one or more molecularly recognizable portions thereon, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof;

a second part which comprises a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

a third part which comprises one or more <u>non-radioactive</u> signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

Serial No.: 08/479,995 Filed: June 7, 1995

Page 23 [(Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

475. (Amended) A composition of matter comprising:

a complex which comprises:

an analyte having one or more molecularly recognizable portions

thereon;

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, said analyte molecularly recognizable portion comprising a biological system selected from the group consisting of a virus or a viral component thereof and a cell or a cellular component thereof, said cell or cellular component thereof comprising a bacterium or a bacterial component thereof, said first portion being selected from the group consisting of an antigen, a polyclonal or a monoclonal antibody, a hormone, a receptor, an enzyme, an allosteric effector, an enzyme substrate, an enzyme cofactor, a protein and a protein receptor, and a second portion comprising one or more nucleic acid sequences or segments; and

one or more non-radioactive signalling entities substantially incapable of binding to or hybridizing with the molecularly recognizable portion on said analyte, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more chemically modified or artificially altered polynucleotides capable of directly or indirectly providing a detectable signal, said direct signal providing signal generating portion being selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound, an enzyme, and said indirect signal providing signal generating portion being selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a polynucleotide sequence capable of recognizing a signal-containing moiety, and a compound capable of binding to an insoluble phase.

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Page 24 [(Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

479. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

(i) a container carrying a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable portion on said analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

a container carrying more than one <u>non-radioacitve</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion nucleic acid sequence or segment, and one or more signal generating portions, each such portion being capable of providing a detectable signal;

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.



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Page 25 ((Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

480. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof: a container carrying a complex which comprises:

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a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with said molecularly recognizable portion, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity second portion, and one or more signal generating portions, each such portion being capable of providing a detectable signal; wherein the ratio of the nucleic acid sequences or segments in the second

portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

Serial No.: 08/479,995 Filed: June 7, 1995

Page 26 ((Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

481. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

a container carrying more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

a container carrying more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion to form a polynucleotide hybrid, and one or more signal generating portions capable of providing a detectable signal;

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

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Page 27 ((Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

482. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof:

more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal generating portions capable of providing a detectable signal;

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

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Page 28 ((Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999)

483. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof: a complex which comprises:

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(i) more than one molecular bridging entity, each such entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and
(ii) more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more signal

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

generating portions capable of providing a detectable signal;

wherein both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the signal generating portions to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

Serial No.: 08/479,995 Filed: June 7, 1995

Page 29 [(Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) - August 25, 1999]

484. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof: a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and more than one non-radioactive signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion, and one or more polynucleotides which have been chemically modified or artificially altered;

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein one or both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

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Page 30 [(Amendment Under 37 C.F.R. §1.115

(In Response To The October 27, 1999 Office Action) August 25, 1999]

485. (Amended) A kit for the detection in a sample of an analyte having one or more molecularly recognizable portions thereon, comprising as components thereof: a complex which comprises:

a molecular bridging entity comprising a first portion capable of recognizing and binding to or hybridizing with a molecularly recognizable portion on an analyte, and a second portion comprising one or more nucleic acid sequences or segments; and

more than one <u>non-radioactive</u> signalling entity, each such entity comprising a nucleic acid portion capable of binding to or hybridizing with said bridging entity nucleic acid second portion to form a polynucleotide hybrid, and one or more polynucleotides which have been chemically modified or artificially altered;

wherein the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity is selected from a number greater than 5 and a number greater than 10; or

wherein one or both the ratio of the nucleic acid sequences or segments in the second portion to the first portion of the molecular bridging entity and the ratio of the one or more chemically modified or artificially altered polynucleotides to the nucleic acid portion in any or all of the signalling entities is selected from a number greater than 1, a number greater than 5 and a number greater than 10.

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